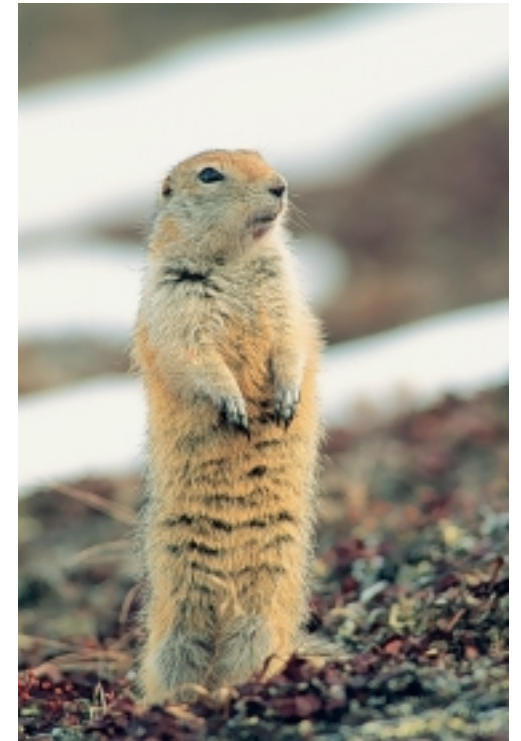
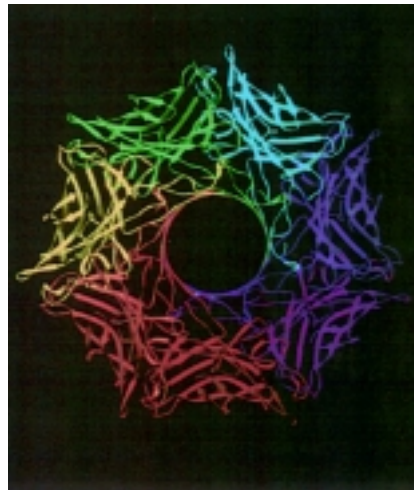
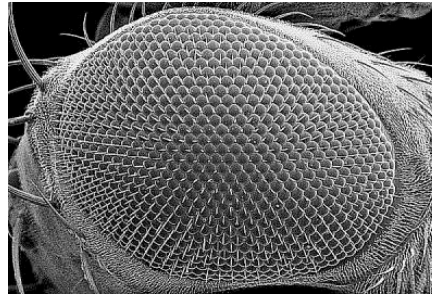
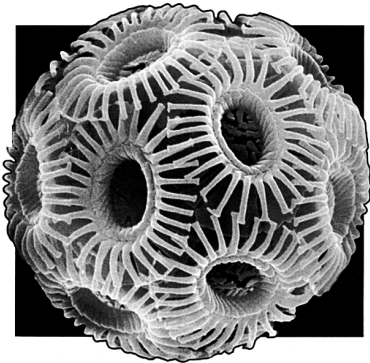


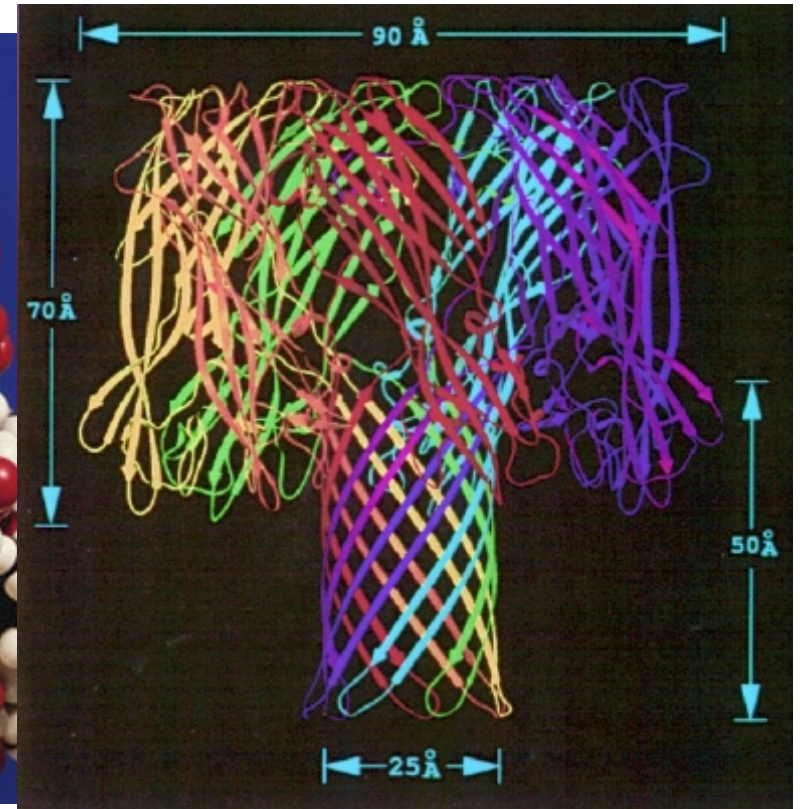
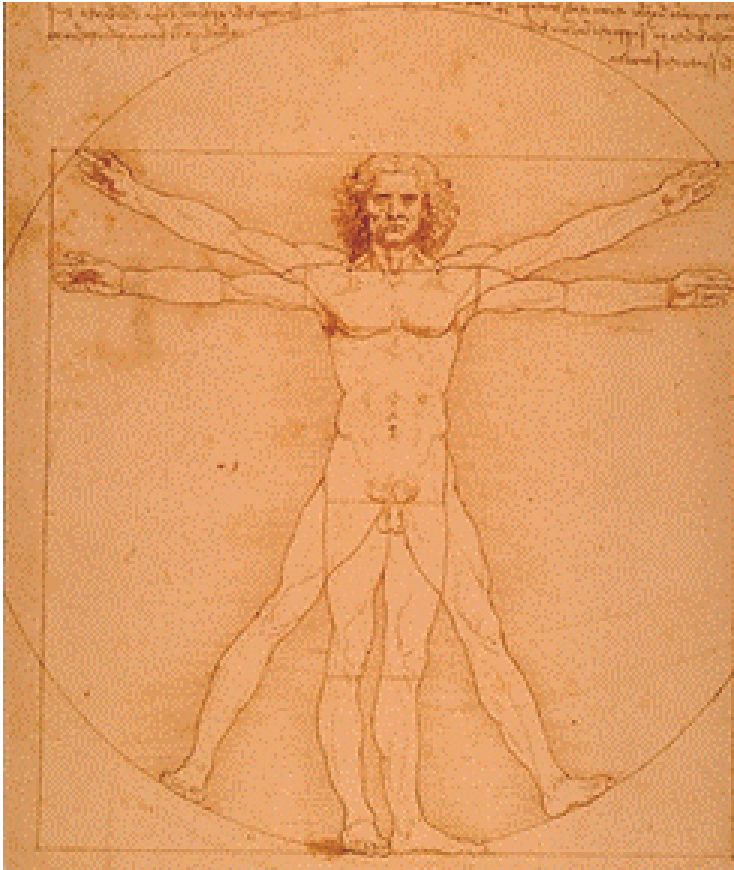
Why and How DARPA/DSO Does Biology

Eric Eisenstadt

4 Billion Years of Biology



~50 Years of Molecular Biology



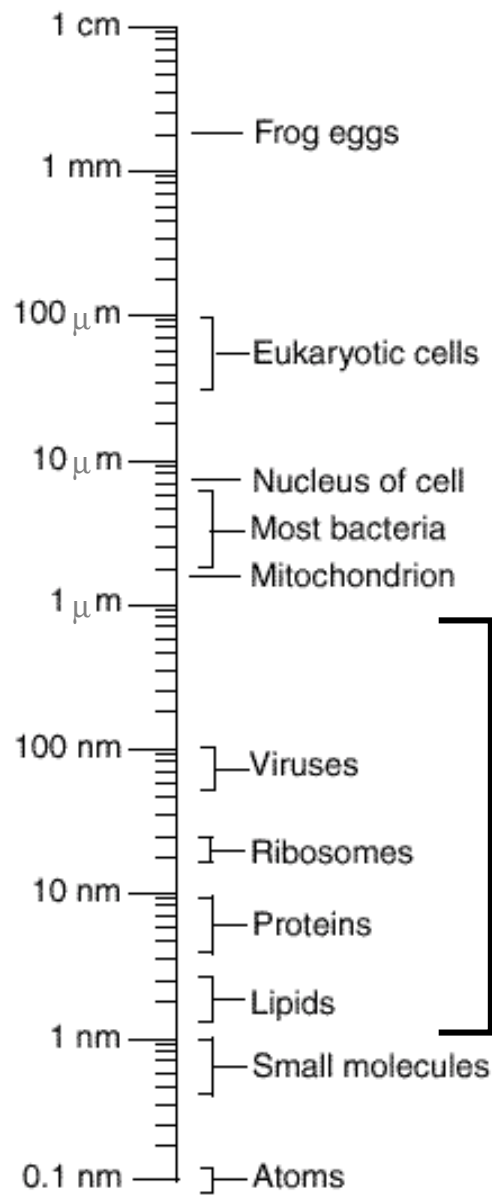
- 1953: Structure of DNA
- 2000: Human genome sequence



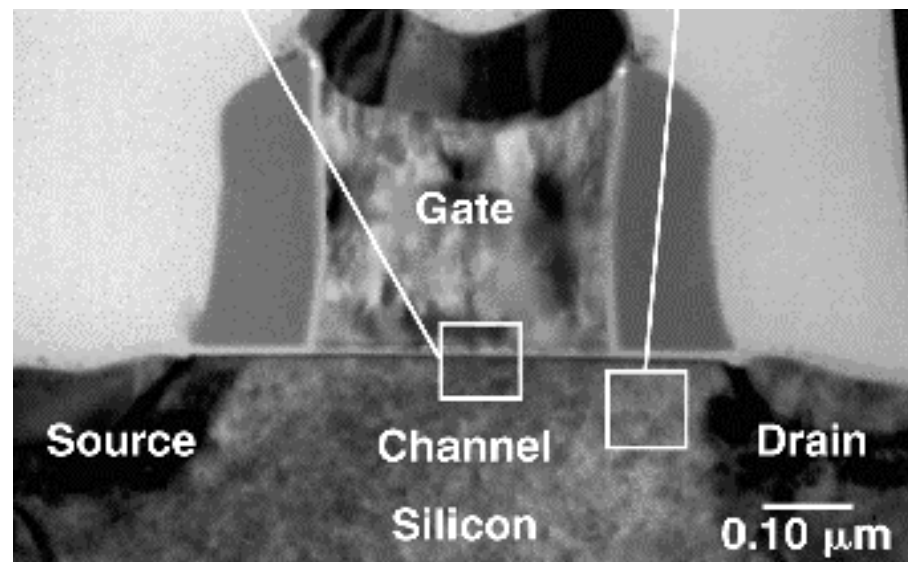
Improved DOD Capabilities via Biology

- Health
- Operations
- Materials synthesis

Physical Maps to Bio



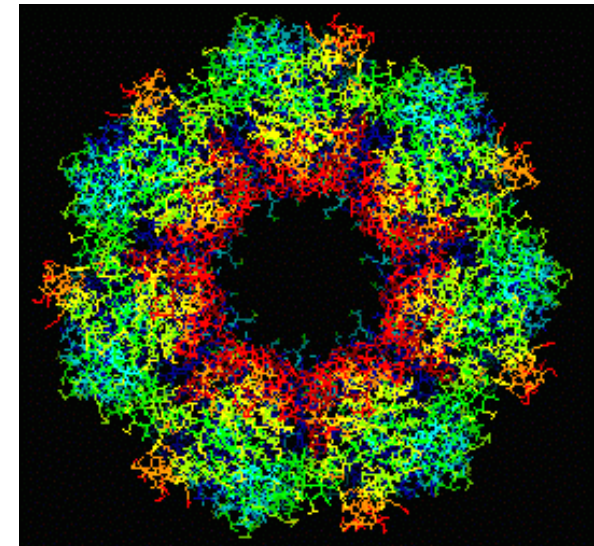
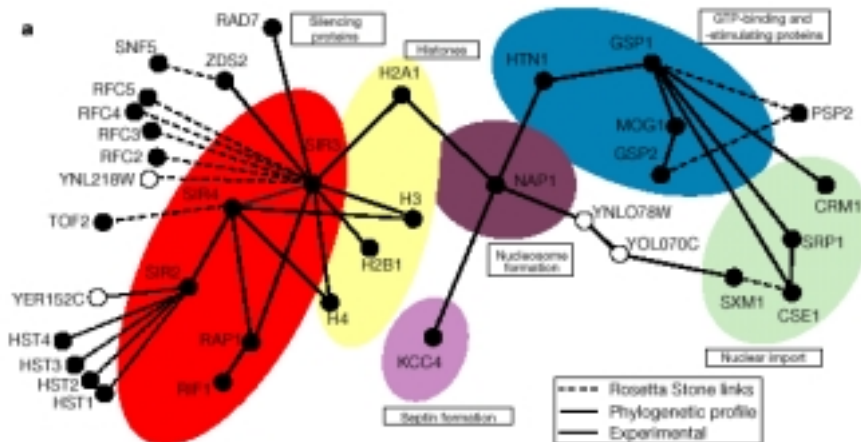
CMOS
elements



Info Maps to Biology

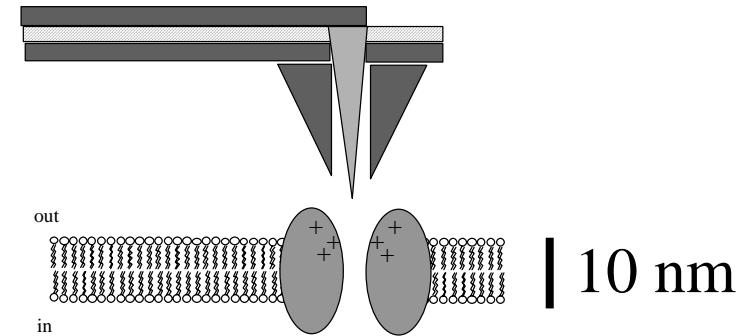


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IIL



Deciphering Biology

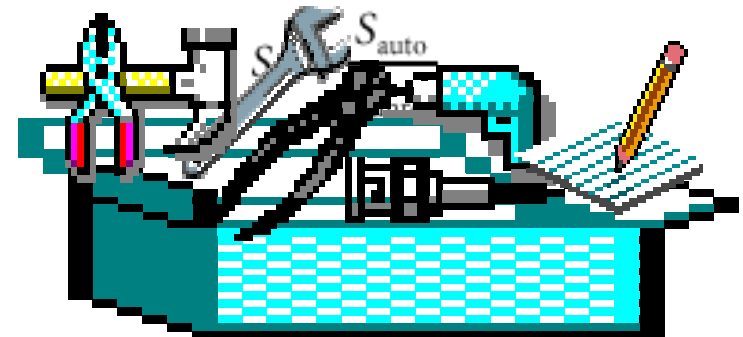
- Interrogate and manipulate biological systems with modern physical devices



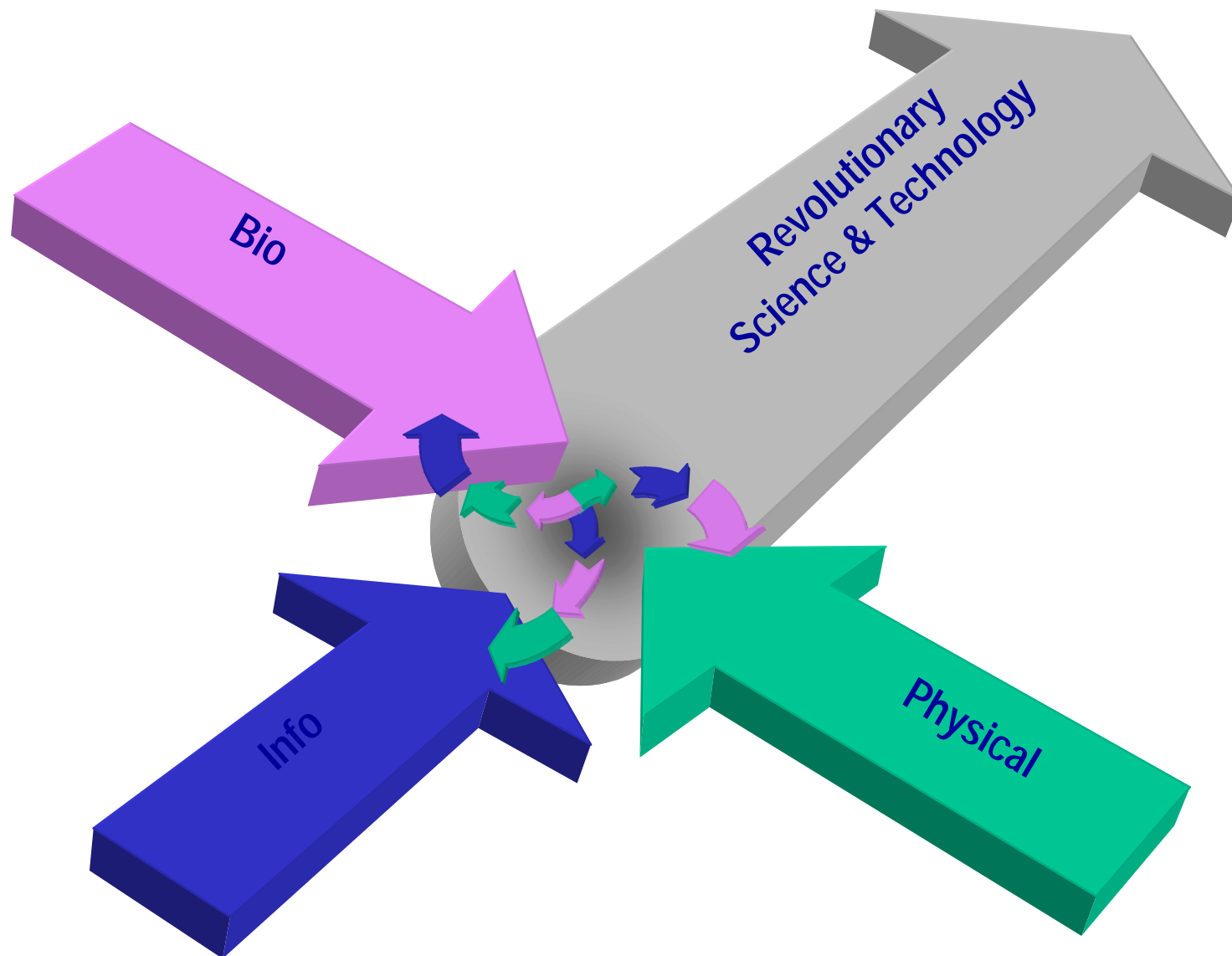
- Analyze, model and simulate with the full arsenal of math and computational tools

$$S_{\text{unreg}} = f'_{\text{unreg}}(R^*) = -k_{\text{deg}}$$

$$S_{\text{auto}} = f'_{\text{auto}}(R^*) = -\frac{nk_p P k_i a k_r}{(1 + k_p P + k_r R^*)^2} - k_{\text{deg}}$$



[Bio:Info:Physical]



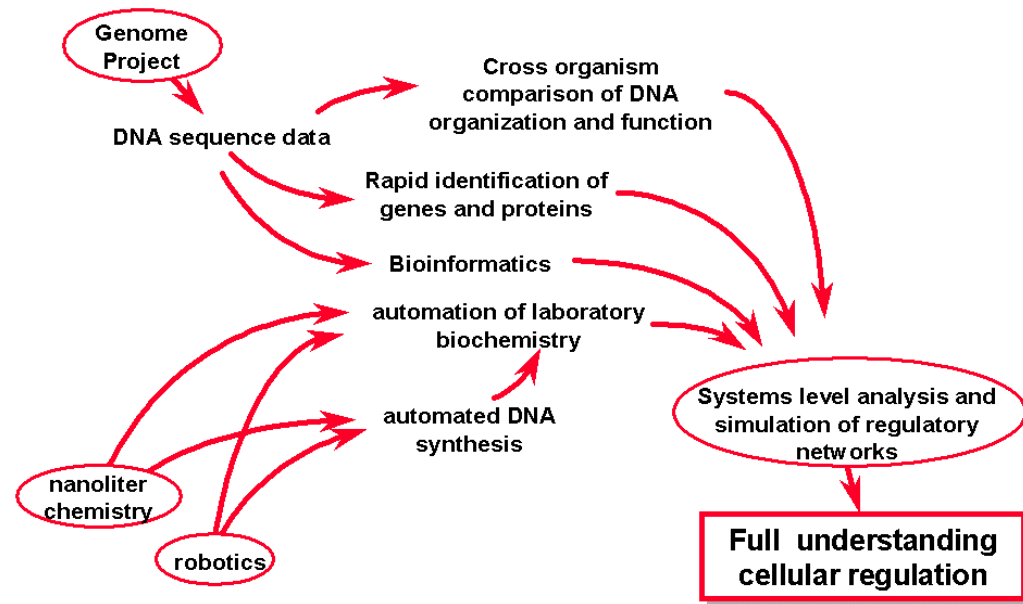
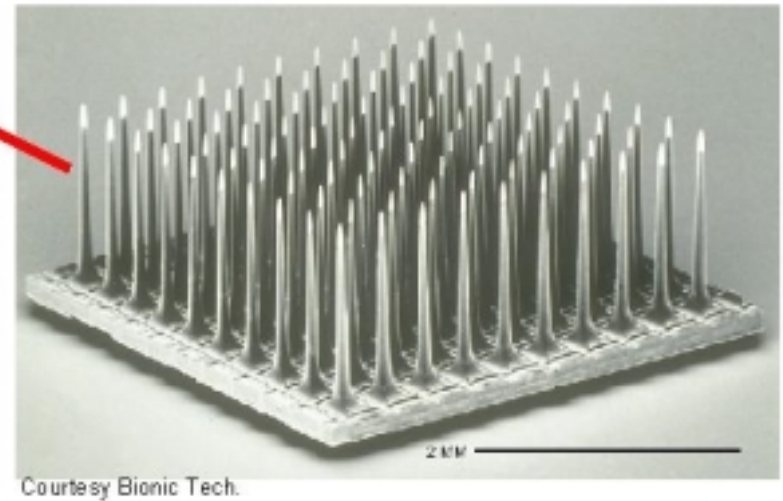
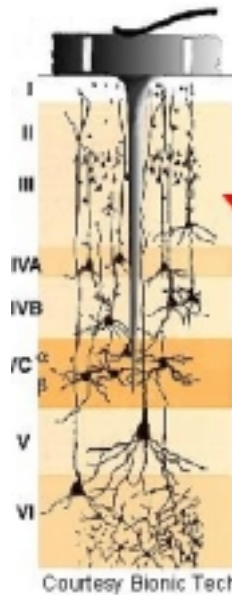


DARPA's Bio:Info:Physical Program

- First phase of DARPA BioFutures
- Fundamental research at universities
- Interdisciplinary
- Attack fundamental limits of understanding complex biological systems via the development and application of new devices and new information tools

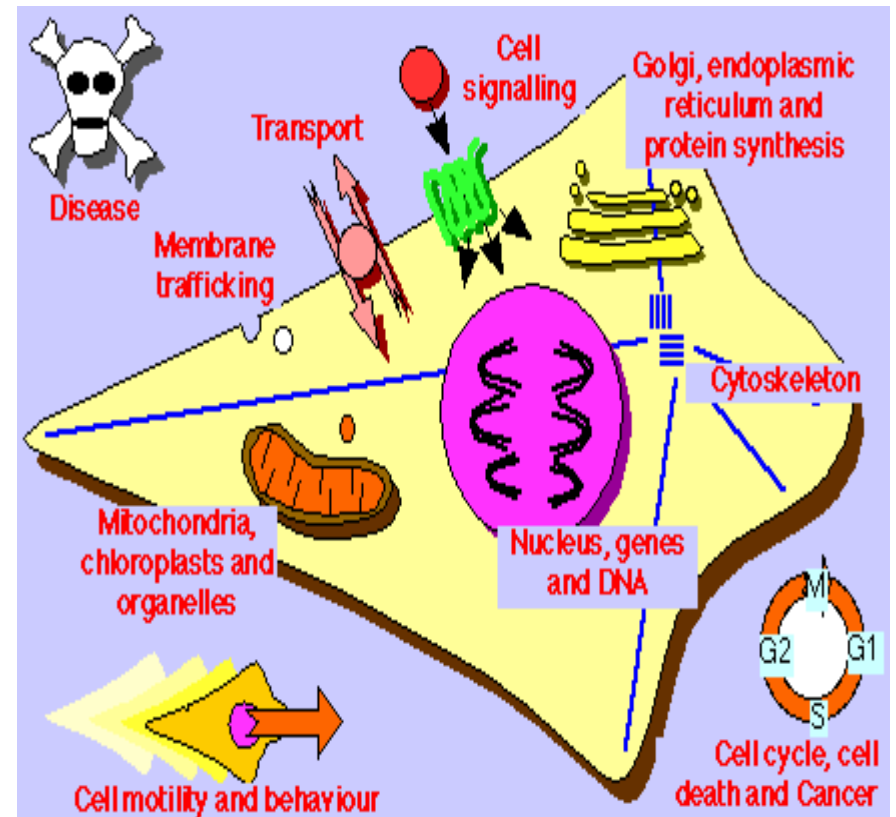
Two Major Themes

- **Neuroprocessing and neurocontrol via high density implantable MEMS devices**
- **Measuring and modeling the dynamic behavior of biological regulatory networks in living cells**



The Cell is a High Information Content Sensor!

- Cell is unit machine in biology responsible for systems level processing
- Cells respond to environment in specific, reproducible and redundant ways
- Cell sensors do not require specific identification of threat
 - Processing will result in identification
 - Amplification of response
- Response is predictive of functional consequences





Tissue Based Biosensors Program Concept

CBW Threat

Physiological Biosensors

Human Health
Risk
Assessment

seconds —→ *minutes* —→ *hours* —→ *days* —→ *years*

- Is it chem or bio?

- Live vs. dead?

- Classification

- Known or unknown

- **Physiological consequences of exposure?**

- **Functional response and mechanism of action?**

- **Long-term consequences of exposure?**

- **Genotoxicity?**

- **Human performance deficits?**

Nature's Metabolic Engineering

You've got questions?

We've got answers...

Performance Specs

- 37° to -5° C Core temps.
- Heart rate: 300 to 7 bpm
- CBF: down to 7% of norm.
- BMR down to <10% of norm.
- 94% genetic homology with humans

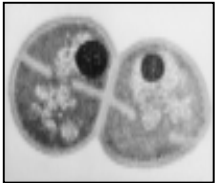


Arctic Ground Squirrel

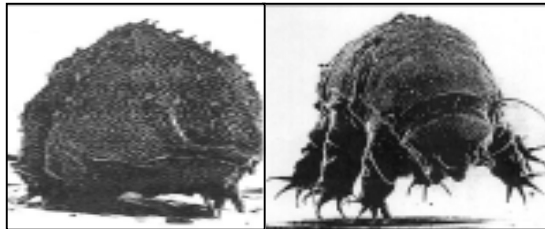
Natural Examples of Metabolic Control and Downregulation

Exploit the lessons learned from “Life on
the Edge”

**Extremophile
bacteria**



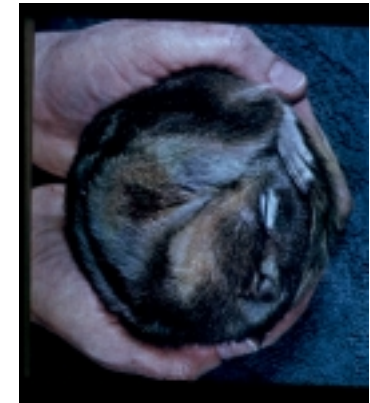
Dried *Tardigrade*



Frozen frog



**Hibernating
squirrel**

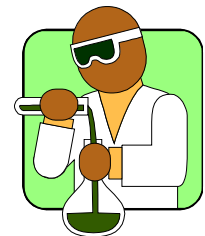
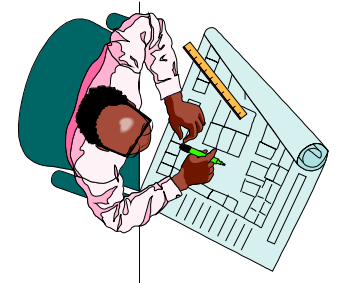


Why now?

- Recent discoveries in stasis strategies, genetics, and gene products now enable the development of a metabolic strategies and systems “toolbox”.

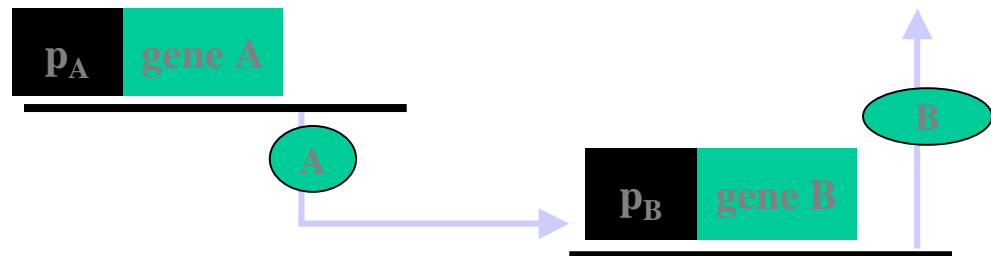
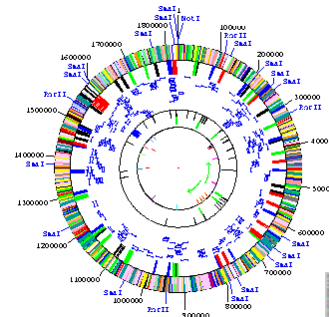
Sequencing Pathogen Genomes

- A genome sequence is a cell's blueprint
- Annotating a genome sequence yields the identity of its unique and common molecular parts
- Knowing the molecular parts permits rational design of countermeasures and detection strategies



A New Era in Biology, a New Era for DARPA

- Molecular anatomy
- Where the parts are
- How the parts work as a system



DARPA's role will be to develop not only new understanding but, more importantly, new biologically inspired systems, tools and devices that enhance DoD and national security